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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,710	02/24/2004	Mark L. Nelson	PAZ-025CPCNRCE2	3651

30623 7590 11/10/2008

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EXAMINER	
HAVLIN, ROBERT H	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
11/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/786,710	NELSON ET AL.	
	Examiner	Art Unit	
	ROBERT HAVLIN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,9-14,18,19,21,23-25,30-40,66,67,82,140-143 and 145-154* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-4,6,7,9-14,19,21,23-26,30-40,56,58-68,82,103-143,145-147 and 149-154.

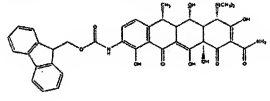
DETAILED ACTION

Status of the claims: Claims 1-4, 6-7, 9-14, 19, 21, 23-26, 30-40, 56, 58-68, 82 and 103-143, 145-147, and 149-154 are pending in the application. Claims 1-2, 9-10, 32, 82, 103-141, 150 and 154 have been amended.

Election / Restriction

The elected group and species is cited from the office action of 1/5/2006:

Acknowledgement is made of Applicant's election (without traverse) of Group I and, for search purposes, the species,



, in a response filed 11/09/2005.

As detailed in the rejection below, no generic claim was found patentable; therefore, the claims remain restricted in scope to the elected species only. Subject matter reading outside the scope of the elected species is hereby withdrawn.

RESPONSE TO APPLICANT REMARKS

Double patenting

The double patenting rejections of claims 1-4, 6-7, 9-14, 19, 21, 23, 24, 30-40, 82, and 140-143, 145-154 are **maintained**. Applicant states they will consider filing a terminal disclaimer upon notice of allowable subject matter.

Claim Rejections - 35 USC § 102

1. Claims 1-4, 6, 11-13, 16, 19, 21 and 82 were rejected under 35 U.S.C. 102(b) as being anticipated by Sum et al. (US 5,430,162). Based on applicant pointing out

distinguishing characteristics between the claims and the prior art (specifically the requirement of X being present) **this rejection is withdrawn**.

2. Claims 140-146, 148-150, and 154 were rejected under 35 U.S.C. 102(b) as being anticipated by Hlavka et al. (US 5,494,903). Based on applicant's amendments cancelling claims and deleting the alternative of alkylamino from the definition of R9a, **this rejection is withdrawn**.

Claim Rejections - 35 USC § 112

Claims 103-139 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant has amended the claims to delete the language referring to "prodrug" therefore **the rejection is withdrawn**.

NEW CLAIM REJECTIONS

Based on the withdrawal of the aforementioned rejections, the examiner expanded the scope of examination beyond the elected species within the generic claim 1 and found the claim unpatentable based on the following rejection.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

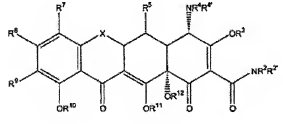
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 7, 11, 18, 23-25, 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barden et al. (J. Med Chem, 1994, v. 37, no. 20, p. 3205-3211) in view of Silverman, R. B. (The Org. Chem. of Drug Design and Drug Action, Academic Press, Inc.: San Diego, 1992, pp. 4-51).

The instant claims are for compounds of the formula I:

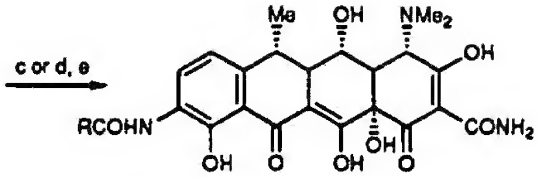


(I)

including species where X is >CHCH3; R2, R2', R3, R7, R8, R10, R11, and R12 are H; R5 is OH; R4, R4' are Me; R9 is NR9cC(=Z')ZR9a; R9c is H; Z and Z' are O; R9a is propyl.

Determining the scope and contents of the prior art

Barden teaches compound 12 shown below and screens several related compounds for biological (antibacterial) activity:



7:R=BrCH2 11:R=C9H19 15:R=Me2NCH2
8:R=H 12:R=MeO 16:R=Et2NCH2
9:R=Me 13:R=(CH2)4NCH2 17:R=t-C4H9NHCH2
10:R=Me2CH 14:R=(CH2)5NCH2 18:R=n-C4H9NHCH2

Which is similar to the claimed compounds when X is >CHCH3; R2, R2', R3, R7, R8, R10, R11, and R12 are H; R5 is OH; R4, R4' are Me; R9 is NR9cC(=Z')ZR9a; R9c is H; Z and Z' are O; **R9a is Me**. The reference also teaches that modifications at the 9a-position varied and increased potency with lengthening of the alkyl chain length (see pages 3206-07).

Silverman teaches drug discovery, design, and development through modifications of the structure of known molecules showing some activity. For example, Silverman teaches on pages 16-18 homologation of carbon chains. Specifically, the method teaches how lengthening a carbon chain (by increasing successive CH2 groups) increases pharmacological effects.

Ascertaining the differences between the prior art and the claims at issue

The difference between the Barden compound and the claims is a single CH2CH2 group at the R9a position (for example changing of methyl to propyl). The

original claim scope read on the Barden compound above, but for claim amendments later excluding it by changing the alternative of alkyl to C3-10 alkyl.

Resolving the level of ordinary skill in the pertinent art.

One of ordinary skill in the art of pharmaceutical development would be well versed in the teachings of references such as Silverman. One of ordinary skill in the art would consider routine and well within their technical grasp the process of altering the substituents on drug molecules and screen them for activity on a large scale to improve potency.

Considering objective evidence present in the application indicating obviousness

Upon reading the teachings of Barden, one of ordinary skill in the art would immediately recognize potential to improve the potency of the compounds taught therein through altering the substituents via homologation. Silverman specifically teaches the homologation methodology and provides the underlying physicochemical motivation of altering the lipophilicity of the molecule which would reasonably be applicable to the compound of Barden. In addition, the Barden compound is a homolog of the instant claims, only differing by successive addition of –CH2- group, thus one of ordinary skill in the art would expect the physical properties of the two compounds to be similar.

This is further supported by caselaw and the MPEP in section 2144.09(II):

> Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195

USPQ 426 (CCPA 1977); see also In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978).

Therefore, because the reference teaches homologs of the instantly claimed compounds and the MPEP states that homologs are presumed to possess similar properties, it would have been obvious to one of ordinary skill in the art to modify the alkyl chain length and arrive at the instant invention.

One of ordinary skill in the art would have been guided by the prior art to make the invention as claimed because Barden teaches the homologous compound, while Silverman teach how to modify the compound to arrive at the instant invention. Therefore, the claims are obvious.

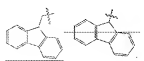
Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 32, and 82 are rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

Claims 1 and 82 contain amendments including deleting part of a proviso and altering the scope of R9a to C3-10-alkyl without sufficient support in the original disclosure. The amendment effectively creates a new subgenus whose entire scope is not supported by sufficient representative species.

Similarly, the amended claim 32 creates an unsupported new subgenus with the amendment:  .

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a

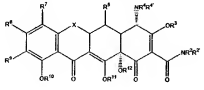
representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

It is noted that in the following the comparison is focused on products and not method of use. It is to be understood, however, that a *prima facie* conclusion of lack of written description for product implies the same conclusion for the process of use. In other words, the process of use cannot be practiced in absence of the product.

I. ***Scope of Claims (based on*** elected ***subject matter)***

Compounds of Formula I:.



(I)

The following variables are claimed in a manner not supported by the disclosure (see below section II):

R^{9a}: for claims 1, 32 and 82

II. Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice support the following definitions:

R^{9a}: the claims as originally filed and the individual species

Reduction to Structural or Chemical Formulas:

The only disclosure, in addition to the species reduced to practice, is in form of a *list* of possible substituents for each variable. This type of disclosure is not viewed to be a representation of any of the species it entails. A"laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Therefore, there is no disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

Furthermore, the instant specification does not disclose any correlation between function and structure. Thus, it is not understood what *specific structural elements* (pertaining to variables R^1-R^3) are *essential* for the activity of the instantly claimed compounds towards glucocorticoid receptor.

III. Analysis of Fulfillment of Written Description Requirement:

In the absence of a correlation between structure (as it pertains to variables) and function, it is not possible to predict what modifications will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1, 32, and 82; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with

the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

No claim is in condition for allowance. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is

(571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner
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